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10/530,789	04/08/2005	Yutaka Tokiwa	SAEG 184.001APC	9374

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EXAMINER	
GOON, SCARLETT Y	

ART UNIT	PAPER NUMBER
1623	

NOTIFICATION DATE	DELIVERY MODE
11/05/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/530,789	TOKIWA ET AL.	
	Examiner	Art Unit	
	SCARLETT GOON	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 July 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,11,13-17 and 37-48* is/are pending in the application.

4a) Of the above claim(s) *11 and 45-48* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,13-17 and 37-44* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This Office Action is in response to Applicants' Amendment and Remarks filed on 2 July 2009 in which claims 2-10, 12 and 18-36 were cancelled, claims 11, 13 and 37 are amended to change the scope and breadth of the claims, and new claims 38-48 are added.

Claims 1, 11, 13-17 and 37-48 are pending in the instant application.

Priority

This application is a National Stage entry of PCT/JP03/13018 filed on 10 October 2003, and claims priority to Japanese patent application No. 2002-297040, filed on 10 October 2002, Japanese patent application no. 2002-353403, filed on 5 December 2002, Japanese patent application no. 2003-117973, filed on 23 April 2003, and Japanese patent application no. 2003-294543, filed on 18 August 2003. A certified copy of each foreign priority document, in Japanese, has been received. No English translation has been provided for any of the foreign priority documents.

Election/Restrictions

Amended claim 11 and newly added claims 45-48 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: Amended claim 11 and newly added claims 45-48 are directed to a method of inhibiting tyrosinase, whereas original claim 11 was drawn to a composition comprising

an arbutin ester according to claim 1. Thus, amended claim 11 and newly added claims 45-48 fall into two different statutory classes.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Moreover, since applicant has received an action on the merits for the inventions as originally filed, according to MPEP § 819, the general policy of the Office is not to permit the Applicant to shift to, or include, additional claims claiming another invention, such as in amended claim 11 and new claims 45-48.

Accordingly, claims 11 and 45-48 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and the product claims are subsequently found allowable, withdrawn process claims that depend from or otherwise require all the limitations of the allowable product claim will be considered for rejoinder. All claims directed to a nonelected process invention must require all the limitations of an allowable product claim for that process invention to be rejoined.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103 and 112. Until all claims to the elected product

are found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowable product claim will not be rejoined. See MPEP § 821.04(b). Additionally, in order to retain the right to rejoinder in accordance with the above policy, applicant is advised that the process claims should be amended during prosecution to require the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder**. Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

Claims 1, 13-17 and 37-44 are examined on its merits herein.

Rejections Withdrawn

Applicant's amendment, filed 2 July 2009, with respect to the rejection of claims 1, 11-17 and 37 under 35 USC § 112, second paragraph, as being indefinite for reciting "an alkylene group" in claims 1 and 13, has been fully considered and is persuasive because the claim has been amended to recite "an alkyl group".

Applicant's amendment, filed 2 July 2009, with respect to the rejection of claim 11 under 35 USC § 112, first paragraph, for lack of scope of enablement, is hereby withdrawn because the claim has been amended from a product claim to a method claim, thereby changing the statutory class of the invention, and resulting in the claim being withdrawn from examination for being drawn to a non-elected invention.

Applicant's amendment, filed 2 July 2009, with respect to the rejection of claims 1, 11-17 and 37 under 35 USC § 112, first paragraph, for failing to comply with the written description requirement, has been fully considered and is persuasive because Table 1-1 and other examples of the disclosure provide sufficient information to show that Applicants were in possession of the claimed invention at the time the application was filed.

In view of the cancellation of claims 2-10, 12 and 18-36, all rejections made with respect to claims 2-10, 12 and 18-36 in the previous Office Action are withdrawn.

These rejections have been **withdrawn**.

The following are new ground(s) or modified rejections necessitated by Applicants' amendment, filed on 2 July 2009, wherein the limitations in pending claim 13 as amended now have been changed; claims 14-17 depend from claim 13, and newly added claims 38-44 are different in breadth and scope from the previously examined claims. The limitations in the amended and newly added claims have been changed and the breadth and scope of those claims have been changed. Therefore, rejections from the previous Office Action, dated 2 March 2009, have been modified and are listed below.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 41 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 41 recites the limitation "6-*O*-decenoyl arbutin" in line 3, "6-*O*-oleoyl arbutin," "6-*O*-benzoyl arbutin," "6-*O*-butanoyl arbutin" and "6-*O*-lauroyl arbutin" in line 4, and "6-*O*-stearoyl arbutin" in line 5. There is insufficient antecedent basis for this limitation in the claim since the formulas for the compounds were previously deleted from amended claim 1.

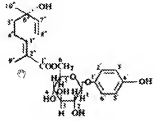
Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1 and 37-40 are rejected under 35 U.S.C. 102(b) as being anticipated by journal publication by Takido *et al.* (of record).

Takido *et al.* disclose a compound called phlebotrichin. Phlebotrichin, compound (2), is a phenolic glucoside and its structure is shown in Figure 1 (p. 224) and below. Phlebotrichin was extracted from fresh leaves of *Viburnum phlebotrichum* with methanol, further chromatographed on silica gel using ethyl acetate, and then recrystallized in ethyl acetate (p. 324, column 1).



It is noted that Takido *et al.* do not teach phlebotrichin as an external preparation for the skin. However, the recitation "external preparation for the skin" in claim 38 is considered to be an "intended use" of the composition, and is therefore not given any patentable weight. Applicant is requested to note that the "intended use" of a composition will not further limit the claims drawn to a composition or product, so long as the prior art discloses the same composition comprising the same ingredients in an effective amount, as that instantly claimed. See, e.g., *Ex parte Masham*, 2 USPQ2d 1647 (1987) and *In re Hack* 114, USPQ 161.

Thus, phlebotrichin and solutions containing the phlebotrichin, disclosed by Takido *et al.*, anticipates claims 1 and 37-40.

Response to Arguments

Applicant's arguments, filed 2 July 2009, with respect to the rejection of claim 1 made under 35 USC § 102(b) as being unpatentable over Takido *et al.*, have been fully considered but they are not persuasive.

Applicants argue that the compound disclosed in the Takido *et al.* reference contains a hydroxyl group, which is not included in the compounds defined in claim 1. This argument is not persuasive because R_1-CH=CH_2, wherein R_1 is a single bond, an alkyl group or an arylene group does not specifically limit the alkyl group to any

substitution or non-substitution. Furthermore, Applicants' Specification as originally filed indicate that "[t]he structure thereof is not limited, and may be straight-chain, branched-chain, cyclic or any other structure" in paragraph [0035] of the published application. Thus, the compound disclosed by Takido *et al.* necessarily anticipates the instant claims.

The rejection is still deemed proper and therefore adhered to.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 13-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over journal publication by Takido *et al.* (of record) as applied to claims 1 and 37-40, further in view of WIPO publication WO2001/79241 to Weiss *et al.* (IDS dated 1 July 2005), in view of publication by Kiyoshi *et al.* (of record), as evidenced by Gordon *et al.* (of record).

The teachings of Takido *et al.* were as disclosed above in the claim rejections under 35 USC § 102. Takido *et al.* do not disclose methods for the synthesis of phlebotrichin.

Weiss *et al.* teach biologically active glycoside esters, methods for their production and the use of these compounds in cosmetic or pharmaceutical

preparations. The biologically active glycoside ester is made by reaction at the primary hydroxyl group of the sugar/glycoside (p. 2, paragraph 8). Preferred monosaccharide glycosides include glucose and arbutin (p. 2, paragraphs 13-14). Suitable fatty acids for esterification include stearidonic acid and 6,9,12,15-octadecatetraenoic acid (p. 2, paragraph 13).

The esterification reaction for the production of the glycoside ester is preferably carried out in the present of a lipase (p. 4, paragraph 4). Suitable enzymatic catalysts for esterification include lipases from Candida antarctica, Candida rugosa, Geotrichum candidum, aspergillus niger, penicillum roqueforti, rhizopus arrhizus and Mucor miehei (p. 4, paragraph 5). To purify the glycoside esters from the enzymatic reaction, an aqueous two-phase extraction procedure with organic solvents such as hexanes, cyclohexane, THF, or diethylether, is employed (p. 4, paragraph 10).

The glycoside ester compounds can be made into cosmetic preparations such as shampoos, lotions, creams, gels, etc. (p. 5, paragraph 1). In addition to the glycoside ester active ingredient, the cosmetic or pharmaceutical composition can further be combined with other active substances, together with one or more inert carriers or diluents (p. 5, paragraph 3).

The synthesis for esterification of arbutin with stearidonic acid is described in Example 3 (p. 5, last paragraph). The reaction is catalyzed with Lipase B from Candida antartica in the presence of molecular sieves, and was complete in 48 hours.

It is noted that Weiss *et al.* do not explicitly teach that the esterification reaction is carried out while performing a dehydration treatment. However, the procedures for the

synthesis of the glycoside esters, disclosed by Weiss *et al.*, involve the use of molecular sieves. As evidenced in the technical bulletin by Gordon *et al.*, molecular sieves are well-known for their drying capacity and are considered a general-purpose drying agent.

Kiyoshi *et al.* teach the preparation of a skin lotion obtained by formulating an acylated derivative of glycosyl-L-ascorbic acid with silicone oil. An acyl ester can be introduced onto glycosyl-L-ascorbic acid via a chemical reaction (p. 3, section 0009) or an enzymatic reaction (p. 4, section 0011). In the case of a chemical reaction, acylating agents that can be used include an acid or acid halide, an anhydride, or an acid ester (p. 3, section 0009). The reaction is generally performed to the exclusion of water, usually in organic solvents such as pyridine, dimethylsulfoxide, and dimethylformamide (p. 4, section 0010). The reaction proceeds regioselectively onto the 6-OH group of the glycosyl moiety. In the case of an enzymatic reaction, a lipase is generally used as the catalyst (p. 4, section 00110). Upon completion of the reaction, the product can be purified by salting out, dialysis, filtration, concentration, fractional precipitation, liquid extraction, or chromatography (p. 5-6, section 0012).

In their examples, Kiyoshi *et al.* describes the synthesis of 2-*O*-α-D-monoglucopyranosyl-6-*O*-octanoyl-L-ascorbic acid. First, 2-glucosylpyranosyl-L-ascorbic acid is dissolved in pyridine. Next, a solution of caprylic anhydride in pyridine is added to the glucosylpyranosyl-L-ascorbic acid solution and the reaction is allowed to proceed for 165 minutes at room temperature. The reaction is stopped by the addition of methanol.

It would have been obvious to one of ordinary skill in the art at the time of the invention to combine the teachings of Takido *et al.*, concerning phlebotrichin, a phenolic glucoside, with the teachings of Weiss *et al.*, regarding biologically active glycoside esters of arbutin or other monosaccharides, methods for their production and the use of these compounds in cosmetic or pharmaceutical preparations, with the teachings of Kiyoshi *et al.*, regarding the preparation of a skin lotion obtained by formulating an acylated derivative of glycosyl-L-ascorbic acid, synthesized either chemically or enzymatically (using a lipase), with silicone oil. Since Weiss *et al.* teach that the glycoside ester compounds have enhanced absorption and penetration properties, and the compound taught by Takido *et al.* is an arbutin glycoside ester, one would have been motivated to develop methods for the synthesis of phlebotrichin. Furthermore, it is noted that Kiyoshi *et al.* do not teach arbutin ester compounds as is taught by Weiss *et al.* and Takido *et al.* However, as Kiyoshi *et al.* and Weiss *et al.* both teach the esterification of the primary hydroxyl group of a glycoside using an enzymatic method that employs a lipase and Weiss *et al.* further teach that the glycoside ester compounds have enhanced absorption and penetration properties in cosmetics (p. 2, paragraph 6), one would have been motivated to search for possible avenues of synthesis of these biologically active glycoside esters as a means to optimize yield and production conditions.

Thus, the claimed invention as a whole is *prima facie* obvious over the combined teachings of the prior art.

Response to Arguments

Applicant's arguments, filed 2 July 2009, with respect to the rejection of claims 13-17 made under 35 USC § 103(a) as being unpatentable over Takido *et al.*, as applied to claim 1, further in view of WIPO publication WO2001/79241 to Weiss *et al.*, in view of publication by Kiyoshi *et al.*, have been fully considered but they are not persuasive.

Applicants argue that the compound disclosed in the Takido *et al.* reference contains a hydroxyl group, which is not included in the compounds defined in claim 1. This argument is not persuasive because R_1-CH=CH_2, wherein R_1 is a single bond, an alkyl group or an arylene group does not specifically limit the alkyl group to any substitution or non-substitution. Furthermore, Applicants' Specification as originally filed indicate that "[t]he structure thereof is not limited, and may be straight-chain, branched-chain, cyclic or any other structure" in paragraph [0035] of the published application. Thus, it would have been *prima facie* obvious for one of ordinary skill in the art to synthesize the compound disclosed by Takido *et al.* using the methods disclosed by Weiss *et al.* and Kiyoshi *et al.*

Applicants additionally argue that the claimed compounds demonstrate unexpected tyrosinase inhibitory activity which would therefore rebut any alleged *prima facie* obviousness rejections. This argument is not persuasive because Applicants' arguments are not directed to the rejection and the closest prior art. As indicated above, the claims encompass the compound disclosed in Takido *et al.* The instant 103 rejection is drawn to how one would synthesize the compound disclosed by Takido *et al.*

Thus, Applicants' arguments of unexpected properties are not applicable to the rejection as the rejection is drawn to how one would synthesize a known compound. A chemical compound and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. See *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). See also MPEP § 2112.01. Applicants are requested to note that arguments of unexpected tyrosinase inhibitory activity would only be applicable in a 103 rejection in which a prior art compound was modified to arrive at the instantly claimed invention, which is not the case in this rejection.

Thus, the rejection is still deemed proper and therefore adhered to.

Allowable Subject Matter

Claims 42-44 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

In view of the rejections to the pending claims set forth above, no claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP

§ 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SCARLETT GOON whose telephone number is 571-270-5241. The examiner can normally be reached on Mon - Thu 7:00 am - 4 pm and every other Fri 7:00 am - 12 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia Jiang can be reached on 571-272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Shaojia Anna Jiang/
Supervisory Patent Examiner, Art Unit 1623

SCARLETT GOON
Examiner
Art Unit 1623